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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,799	05/01/2001	Richard T. Wyatt	157/48457	2915

7590 07/14/2003

Ronald I Eisentein
Nixon Peabody
101 Federal Street
Boston, MA 02110

EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/14/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/446,799	Applicant(s) WYATT ET AL.	
	Examin r Bao Qun Li	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6 and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

This is a response to the amendment, paper No. 17, filed 04/23/03. Claims 1, 4, 6, and 14 have been amended. Claims 5 and 7-13 are canceled. New claims 15-16 have been added. Claims 1-4, 6 and 14-16 are pending and considered by the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

1. Claims 1-3, 14 are still rejected under 35 U.S.C. 112, second paragraph on the same ground as stated in the previous Office Action, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

2. Claim 1 is still unclear for defining which modified gp120 polypeptide is because claims still fail to define which "portion of at least two conserved regions" is referred and which site is the chemokine-binding site.

3. Applicants argue that the precise deletion in the particular portion does not need to be defined because applicants use a functional language to limit what regions must be present.

4. Applicants' argument has been respectfully considered; however, it is not found persuasive. The claimed invention is drawn to a polypeptide, the precise structure of the polypeptide has to be defined.

Claim Rejections - 35 USC § 112

5. Claims 1-3 and 14 are still rejected under 35 U.S.C. 112, first paragraph, because the specification on the same ground as stated in the previous Office, while being enabling for making some recombinant HIV gp120 having a glycosylation sites modification at 196, 276, 301 and 386 that do not change the 3-demisional structure for binging to CD4, does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

6. Applicants argue that examiner's statement of alteration of glycosylation sites may affect the CD4 receptor binding activity that is irrelevant for the present application.

7. Applicants' argument has been considered; however, it is not found persuasive because the maintenance of CD4bs or a CD4i epitope is the limitation of the claimed invention and these epitopes are directed to the CD4 binding. Therefore, the specification has to teach that all claimed gp120 polypeptides are able to have such characteristics.

8. Furthermore, Applicants argue that in light of the teaching from the prior art, a skilled artisan would also know which four sites to use. For example, the specification explicitly teach that positions 197, 276, 301 and 386 are used.

9. Applicants' argument has been fully considered; however, it is not found persuasive because the specification does not teach any four sites are intended and prior art does not teach every glycosylation site around that region is intended.

10. Moreover, the rejected claims 1-3 do not limit the claimed produce only having that four particular positions modified. They would rather directed to any or all glycosylation sites around that region.

11. Considering the broadly claimed scope and limited disclosure, it is still concluded that an undue experimentation is required for a skilled artisan to practice the full scope of the claimed invention. Therefore, the rejection is maintained.

Double Patenting

12. Claims 1-3 are still provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 09/446,820 because Applicants has already acknowledged the issue raised by the previous Office Action; however Applicants are not like to do the terminal disclaimer at the this time. Since Applicants does not raise any objection against this issue, the rejection is maintained.

13. Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 and disclosure of the specification of U.S. Patent No. 5,817,316. Since applicants did not response to this issue, the rejection is maintained.

14.

In the instant case, Sodroski et al. disclose an immunogenic gp120 polypeptide from HIV-1, HIV-2 and SIV comprising the conserved regions, which has at least one of variable regions V1-V3 deleted and replaced by a linker sequence, wherein the linker sequence comprising one to eight amino acids and said linker sequence maintains the overall 3-dimensional structure of the gp120 by permitting turns in the tertiary structure. The linker sequence in comprised of amino acid residues selected from the group consisting of Pro. Glu. And Ala (claims 1-11). The mutated gp120 polypeptide has different sequence structure compared to the wild type, therefore, the glycosylation sites are altered compared with the original sequence. The removal of the variable regions increases the exposure of the discontinuous epitope but maintain its 3-dimesional structure of discontinuous conserved epitope of the wild-type gp120, CD4 binding activity (se entire document, especially, the lines 49-60 on col. 6).

Claim Rejections - 35 USC § 102

15. Claims 1-3 are still rejected under 35 U.S.C. 102(e) on the same ground as stated in the previous Office Action, as being anticipated by Sodroski et al. (US Patent No. 5,817,316A).

16. Applicants admitted that Sodroski et al. teach a modified gp120 polypeptide comprising conserved region which has variable region deletion while maintaining the overall three dimensional structure of the gp120 protein. However, Applicants argue that Sodroski et al. does not teach or disclose removing the specified four glycosylation sites

17. Applicants' argument has been fully considered; however, it is not found persuasive because the limitation of the specified 4 glycocylation sites is only recited in claims 4-6 and claims 1-3 are still broadly read on the same product as it is in the prior art. Therefore, this rejection is still maintained for claims 1-3.

18. Claims 1-3 are still rejected under 35 U.S.C. 102(a) on the same ground as stated in the previous Office Action as being anticipated by Cao et al. (J. Virol. 1997, Vol 71, pp. 9808-9812).

19. Applicants argue that Cao et al. does not teach or suggest the desirable mutation in the specified glycosylation sites.

20. Applicants' argument has been fully considered; however, it is not found persuasive because the specified 4 glycosylation sites is only recited in claims 4-6 and claims 1-3 are still broadly read on the same product as it is in the prior art. Therefore, this rejection is still maintained for claims 1-3.

21. Claims 1-4 are still rejected under 35 U.S.C. 102(b) on the same ground as stated in the previous Office Action as being anticipated by Wyatt et al. (J. Virol. 1997, Vol. 71, pp. 9722-9731).

22. Applicants argue that Wyatt et al. does not teach removal of the specific glycosylation sites.

23. Applicants' argument has been fully considered; however, it is not found persuasive because the specified 4 glycosylation sites is only recited in claims 4-6 and claims 1-3 are still broadly read on the same product as it is in the prior art. Therefore, this rejection is still maintained for claims 1-3.

24. Claims 1-4 are still rejected under 35 U.S.C. 102(b) on the same ground as stated in the previous office action as being anticipated by Binley et al. (AIDS RESEARCH AND HUMAN RETROVIRUSES 1997, Vol. 14, p. 191-198).

25. Applicants argue that Binley fails to provide any teaching regarding the desirability of the four critical glycosylation sites.

26. Applicants' argument has been fully considered; however, it is not found persuasive because the specified 4 removable glycosylation sites is only recited in claims 4-6 and claims 1-3 are still broadly read on the same product as it is in the prior art. Therefore, this rejection is still maintained for claims 1-3.

27. Claims 1-4 and 14 are still rejected under 35 U.S.C. 102(b) on the same ground as stated in the previous Office Action as being anticipated by Bolmstedt et al. (J. Gene Virol. 1991, Vol. 72, pp. 1269-1277).

28. Applicants argue that Bolmstedt's disclosure are not the deletion of present invention.

29. Applicants' argument has been fully considered; however, rejection claims 1-3 do not limit the deletions at any particular sites. Since Bolmstedt et al. also teach that the mutations do not change the cell surface CD4-binding activity and other 3 dimensional structure and discontinuous epitopes (See entire document), the claimed invention is still anticipated by the cited reference.

30. Claims 1-3 are still rejected under 35 U.S.C. 102(b) on the same ground as stated in the previous Office Action as being anticipated by Essex et al. (WO 93/17705A1).

31. Applicants argue that the gp120 variants disclosed by Essex et al. does not teach or suggest any the particular sites of 386, 197, 276 and 301.

32. Applicants' argument has been fully considered; however, rejection claims 1-3 do not limit the deletions at any particular sites of 386, 197, 276 and 301. Since Essex et al. also teach that the mutated envelope proteins do not change the CD4-binding region (lines 13 on page 16 to line 28 on page 17) and the mutated gp120still maintains 3-dimetional structure of the discontinuous epitope of CD4bs and is able to bind CD4bs as well as induce the antibody response in the host (claims 1-14). Therefore, the claimed invention is still anticipated by the cited reference.

33. Claims 1-3 are still rejected under 35 U.S.C. 102(b) on the same ground as stated in the previous Office Action as being anticipated by Pollard et al. (EMBO Journal 1992, Vol. 11, pp. 585-591).

34. Applicants argue that Pollard et all teach a gp120 with variable loop deletion, in which there is no teaching regarding to the specific removal of particular glycosylation sites.

35. Applicants' argument has been fully considered; however, rejection claims 1-3 do not limit the deletions at any particular sites. Since the HIV gp 120 polypeptide disclosed by Pollard et al. comprises the conserved regions and mutations in the regions that CD4 and CXCR4 or CCR5 bind. Moreover, the mutated gp120 polypeptide still contains the 3-demisional structure of the discontinue epitope CD4bs and able to induce immune responses once those polypeptide are injected into the animals (see entire document). Therefore, the claimed invention is still anticipated by the cited reference.

36. Claims 1-3 are still rejected under 35 U.S.C. 102(b) on the same ground as stated in the previous Office Action as being anticipated by Lekutis et al. (Journal of Acquired Immune Deficiency Syndromes 1992, Vol. 5, pp. 78-81).

37. Applicants argue that the site which are mutated in the gp120 of Lekutis are not near the position of the discontinuous CD4 binding sites, but rather are cystines, involved in disulfide bond formation. Thus, it is clear that none of these specific residues could be glycosylation sites of the present invention.

38. Applicants' argument has been respectfully considered; however, it is not found persuasive because the rejection claims do not specify which CD4 binding sites are. The mutation sites disclosed by Lekutis et al. is related to the CD4 binding activity. Therefore, it is considered as sites proximal to the CD4 binding site and the modified gp120 molecule disclosed by Lekutis et al. does not change the CD4 binding abilities, the claimed invention is still anticipated by the cited reference.

Conclusion

The claims 4, 6, 15 and 16 are free of prior art. However, they are no in the condition for allowance due to they are dependent on a rejected claims. If the claims were amended to be an independent form with all limitation as recited in the present form, the claimed subject matter would be allowed.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

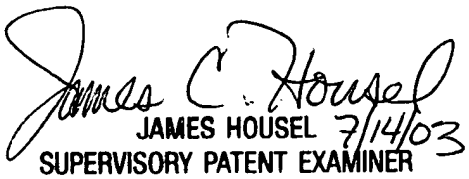
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
June 30, 2003



JAMES HOUSEL 7/14/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600